Complete Summary

GUIDELINE TITLE

Antithrombotic therapy in valvular heart disease -- native and prosthetic: the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy.

BIBLIOGRAPHIC SOURCE(S)

Salem DN, Stein PD, Al-Ahmad A, Bussey HI, Horstkotte D, Miller N, Pauker SG. Antithrombotic therapy in valvular heart disease--native and prosthetic: the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. Chest 2004 Sep;126(3 Suppl):457S-82S. [234 references] PubMed

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Salem DN, Daudelin HD, Levine HJ, Pauker SG, Eckman MH, Riff J. Antithrombotic therapy in valvular heart disease. Chest 2001 Jan;119(1 Suppl):207S-219S.

Stein PD, Alpert JS, Bussey HI, Dalen JE, Turpie AG. Antithrombotic therapy in patients with mechanical and biological prosthetic heart valves. Chest 2001 Jan;119(1 Suppl):220S-227S.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Systemic embolism associated with:

- Rheumatic mitral valve disease (mitral stenosis and/or mitral regurgitation) with atrial fibrillation (AF)
- Mitral valve prolapse (MVP)
- Mitral annular calcification (MAC) and nonrheumatic mitral regurgitation
- Aortic valve and aortic arch disorders
- Prosthetic heart valves (mechanical prosthetic heart valves and bioprosthetic valves)
- Infective endocarditis
- Nonbacterial thrombotic endocarditis (NBTE)
- Withdrawal of anticoagulation therapy prior to surgery

GUIDELINE CATEGORY

Prevention

CLINICAL SPECIALTY

Cardiology
Family Practice
Internal Medicine
Pulmonary Medicine

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

- To examine the risks of thromboembolism in various forms of native valvular heart disease as well as mechanical and bioprosthetic heart valve replacements, and suggest strategies for using antithrombotic drugs in each disease
- To provide evidence-based recommendations for using antithrombotic drugs for various forms of valvular heart disease in order to prevent systemic embolism

TARGET POPULATION

Patients (particularly in ambulatory settings) with various forms of valvular heart disease, including:

- Rheumatic mitral valve disease (mitral stenosis and/or mitral regurgitation)
- Mitral valve prolapse (MVP)
- Mitral annular calcification (MAC) and nonrheumatic mitral regurgitation
- Aortic valve and aortic arch disorders
- Infective endocarditis
- Nonbacterial thrombotic endocarditis (NBTE)

Those patients with mechanical prosthetic or bioprosthetic heart valves

INTERVENTIONS AND PRACTICES CONSIDERED

Prevention of Systemic Embolism

Pharmacologic Interventions

1. Vitamin K antagonists, including warfarin therapy
2. Antiplatelet agents (APA), including aspirin therapy
3. Warfarin therapy in combination with aspirin, dipyridamole, ticlopidine, or clopidogrel
4. Heparin therapy
    - Intravenous (IV) or subcutaneous (SC) unfractionated heparin
    - Low molecular weight heparin (LMWH)
5. Withdrawal of anticoagulation therapy prior to surgery
6. Withholding long-term antithrombotic therapy and long-term warfarin therapy in selected patients

Monitoring

1. International normalized ratio (INR)
2. Transesophageal echocardiography (TEE)

MAJOR OUTCOMES CONSIDERED

- Effectiveness of antithrombotic therapy in preventing systemic embolism
- Risks of adverse events, such as bleeding
- Cost effectiveness of antithrombotic therapy in preventing systemic embolism in target population
- Mortality

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Process of Searching for Evidence

Defining the clinical question provided the framework for formulating eligibility criteria that guided the search for relevant evidence. Prior to searching for the evidence, methodological experts and librarians reviewed each question to ensure that the librarians could derive a comprehensive search strategy.

In specifying eligibility criteria, authors not only identified patients, interventions, and outcomes, but also methodological criteria. For most therapeutic studies, authors restricted eligibility to randomized controlled trials (RCTs).

For many questions, RCTs did not provide sufficient data, and article authors also included observational studies. This was also true when randomized trials were

not the most appropriate design to use for addressing the research question. In particular, randomized trials are not necessarily the best design to understand risk groups (e.g., the baseline or expected risk of a given event for certain subpopulations). Because there are no interventions examined in questions about prognosis, one replaces interventions by the exposure, which is time.

Identifying the Evidence

To identify the relevant evidence, a team of librarians at the University at Buffalo conducted comprehensive literature searches. For each question the authors provided, the librarians developed sensitive (but not specific) search strategies, including all languages, and conducted separate searches for systematic reviews, RCTs, and, if applicable, observational studies. The librarians searched the Cochrane Database of Systematic Reviews, the Database of Abstracts of Reviews of Effectiveness and Cochrane Register of Controlled Trial, the ACP Journal Club, MEDLINE, and Embase for studies published between 1966 and June 2002 in any language. To filter MEDLINE and Embase search results for RCT evidence, the librarians used the search strategy developed by the Cochrane Collaboration (full strategy available in Appendix online at: http://www.chestjournal.org/content/vol126/3_suppl_1).

For observational studies, they restricted their searches to human studies. Searches were not further restricted in terms of methodology. While increasing the probability of identifying all published studies, this sensitive approach resulted in large number of citations for many of the defined clinical questions. Therefore, trained research assistants screened the citation list developed from the search and removed any apparently irrelevant citations. These irrelevant citations included press news, editorials, narrative reviews, single case reports, animal studies (any nonhuman studies), and letters to the editor. Authors included data from abstracts of recent meetings if reporting was transparent and all necessary data for the formulation of a recommendation were available. The guideline developers did not explicitly use Internet sources to search for research data.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

The rating scheme framework captures the trade-off between benefits and risks (1 or 2) (and the methodological quality of the underlying evidence (A, B, C+, or C). See "Rating Scheme for the Strength of the Recommendations."

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Summarizing Evidence

The electronic searches also included searching for systematic reviews. If authors were satisfied with a recent high-quality systematic review, evidence from that review provided a foundation for the relevant recommendation.

Pooled analyses from high-quality systematic reviews formed, wherever possible, the evidence base of the recommendations. Pooling offers the advantage of obtaining more precise estimates of treatment effects and allows for a greater generalizability of results. However, pooling also bears the risk of spurious generalization. In general, the summary estimates of interest were the different types of outcomes conveying benefit and downsides (i.e., risk, burden, and cost).

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus (Consensus Development Conference)

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The strength of any recommendation depends on the following two factors: the trade-off between the benefits and the risks, burdens, and costs; and the strength of the methodology that leads to the treatment effect. The guideline developers grade the trade-off between benefits and risks in the two categories: 1, in which the trade-off is clear enough that most patients, despite differences in values, would make the same choice; and 2, in which the trade-off is less clear, and individual patients' values will likely lead to different choices.

When randomized trials provide precise estimates suggesting large treatment effects, and the risks and costs of therapy are small, treatment for average patients with compatible values and preferences can be confidently recommended.

If the balance between benefits and risks is in doubt, methodologically rigorous studies providing Grade A evidence and recommendations may still be weak (Grade 2). Uncertainty may come from less precise estimates of benefit, harm, or costs, or from small effect sizes.

There is an independent impact of validity and consistency, and the balance of positive and negative impacts of treatment on the strength of recommendations. In situations in which there is doubt about the value of the trade-off, any recommendation will be weaker, moving from Grade 1 to Grade 2.

Grade 1 recommendations can only be made when there is a relatively clear picture of both the benefits and the risks, burdens, and costs, and when the balance between the two clearly favors recommending or not recommending the

intervention for the typical patient with compatible values and preferences. A number of factors can reduce the strength of a recommendation, moving it from Grade 1 to Grade 2. Uncertainty about a recommendation to treat may be introduced if the following conditions apply: (1) the target event that is trying to be prevented is less important (confident recommendations are more likely to be made to prevent death or stroke than asymptomatic deep vein thrombosis); (2) the magnitude of risk reduction in the overall group is small; (3) the probability of the target event is low in a particular subgroup of patients; (4) the estimate of the treatment effect is imprecise, as reflected in a wide confidence interval (CI) around the effect; (5) there is substantial potential harm associated with therapy; or (6) there is an expectation for a wide divergence in values even among average or typical patients. Higher costs would also lead to weaker recommendations to treat.

The more balanced the trade-off between benefits and risks, the greater the influence of individual patient values in decision making. Virtually all patients, if they understand the benefits and risks, will take aspirin after experiencing a myocardial infarction (MI) or will comply with prophylaxis to reduce the risk of thromboembolism after undergoing hip replacement. Thus, one way of thinking about a Grade 1 recommendation is that variability in patient values is unlikely to influence treatment choice in average or typical patients.

When the trade-off between benefits and risks is less clear, individual patient values may influence treatment decisions even among patients with average or typical preferences.

Grade 2 recommendations are those in which variation in patient values or individual physician values will often mandate different treatment choices, even among average or typical patients. An alternative, but similar, interpretation is that a Grade 2 recommendation suggests that clinicians conduct detailed conversations with patients to ensure that their ultimate recommendation is consistent with the patient's values.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Grade of Recommendation	Clarity of Risk/Benefit	Methodological Strength of Supporting Evidence	Implications
1A	Clear	Randomized controlled trials (RCTs) without important limitations	Strong recommendation; can apply to most patients in most circumstances without reservation
1C+	Clear	No RCTs, but strong RCT	Strong recommendation;

Grade of Recommendation	Clarity of Risk/Benefit	Methodological Strength of Supporting Evidence	Implications
		results can be unequivocally extrapolated, or overwhelming evidence from observational studies	can apply to most patients in most circumstances
1B	Clear	RCTs with important limitations (inconsistent results, methodological flaws*)	Strong recommendation; likely to apply to most patients
1C	Clear	Observational studies	Intermediate-strength recommendation; may change when stronger evidence is available
2A	Unclear	RCTs without important limitations	Intermediate-strength recommendation; best action may differ depending on circumstances or patients' or societal values
2C+	Unclear	No RCTs, but strong RCT results can be unequivocally extrapolated, or overwhelming evidence from observational studies	Weak recommendation; best action may differ depending on circumstances or patients' or societal values
2B	Unclear	RCTs with important limitations	Weak recommendation; alternative

Grade of Recommendation	Clarity of Risk/Benefit	Methodological Strength of Supporting Evidence	Implications
		(inconsistent results, methodological flaws*)	approaches likely to be better for some patients under some circumstances
2C	Unclear	Observational studies	Very weak recommendation; other alternatives may be equally reasonable

*These situations include RCTs with both lack of blinding and subjective outcomes, where the risk of bias in measurement of outcomes is high, or RCTs with large loss to follow-up.

COST ANALYSIS

While conference participants agreed that recommendations should reflect economic considerations, incorporating costs is fraught with difficult challenges. For most recommendations, formal economic analyses are unavailable. Even when analyses are available, they may be methodologically weak or biased. Furthermore, costs differ radically across jurisdictions, and even sometimes across hospitals within jurisdictions.

Because of these challenges, the guideline developers consider economic factors only when the costs of one therapeutic option over another are substantially different within major jurisdictions in which clinicians make use of these recommendations. As a result, in jurisdictions in which resource constraints are severe, alternative allocations may serve the health of the public far better than some of the interventions that are designated as Grade 1A. This will likely be true for all less industrialized countries and, with the increasing promotion of expensive drugs with marginal benefits, may be increasingly true for wealthier nations. Furthermore, recommendations change (either in direction or with respect to grade) only when the guideline developers believe that costs are high in relation to benefits. Instances in which costs have influenced recommendations are labeled in the "values and preferences" statements associated with the recommendation.

Mitral Valve Prolapse (MVP)

The dilemma of cost-effective antithrombotic therapy in patients with MVP would best be solved by a reliable means of identifying the small cohort of patients at high risk for thromboembolism. In a retrospective study of 26 patients with MVP, Steele et al reported that platelet survival time was significantly shortened in all 5

patients with a history of thromboembolism, but this abnormality was also observed in one third of the patients without thromboembolism. Future studies of the clinical and laboratory characteristics of MVP patients may succeed in reducing the fraction of patients at risk.

Withdrawal of Anticoagulation Therapy Prior to Surgery

Patients with valvular heart disease receiving oral anticoagulant (OAC) therapy who require surgical procedures present special problems related to withholding and restarting anticoagulation therapy. The risks of bleeding versus thromboembolism as well as the costs must be carefully balanced. Eckman et al used decision analysis to examine the cost-effectiveness of varying strategies for treating patients with prosthetic heart valves undergoing noncardiac surgery. These authors concluded the marginal cost of prolonging hospitalization to administer heparin was prohibitively high, except when the patient has "the most thrombogenic of valves."

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

The guideline authors formulated draft recommendations prior to the conference that served as the foundation for authors to work together and critique the recommendations. Drafts of all articles including draft recommendations were available for review during the conference. A representative of each article presented potentially controversial issues in their recommendations at plenary meetings. Article authors met to integrate feedback, to consider related recommendations in other articles, and to revise their own guidelines accordingly. Authors continued this process after the conference until they reached agreement within their groups and with other author groups who had provided critical feedback. Finally, the editors of this supplement harmonized the articles and resolved remaining disagreements through facilitated discussion.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

The rating scheme is defined at the end of the "Major Recommendations" field.

Rheumatic Mitral Valve Disease

Rheumatic Mitral Valve Disease with Atrial Fibrillation (AF) or a History of Systemic Embolism

For patients with rheumatic mitral valve disease and AF, or a history of previous systemic embolism:

1. The guideline developers recommend long-term oral anticoagulant (OAC) therapy (target international normalized ratio [INR], 2.5; range, 2.0 to 3.0) (Grade 1C+).

For patients with rheumatic mitral valve disease and AF, or a history of previous systemic embolism:

2. The guideline developers suggest clinicians not use concomitant therapy with OAC and antiplatelet agent (APA) (Grade 2C).

   Underlying values and preferences: This recommendation places a relatively high value on avoiding the additional bleeding risk associated with concomitant OAC and antiplatelet therapy.

For patients with rheumatic mitral valve disease with AF or a history of systemic embolism who suffer systemic embolism while receiving OACs at a therapeutic INR:

3. The guideline developers recommend adding aspirin, 75 to 100 mg/d (Grade 1C). For those patients unable to take aspirin, the guideline developers recommend adding dipyridamole, 400 mg/d, or clopidogrel (Grade 1C).

Patients with Mitral Valve Disease in Sinus Rhythm

1. In patients with rheumatic mitral valve disease and normal sinus rhythm with a left atrial diameter >5.5 cm, the guideline developers suggest long-term vitamin K antagonist therapy (target INR, 2.5; range, 2.0 to 3.0) [Grade 2C].

   Underlying values and preferences: This recommendation places a relatively high value on avoiding systemic embolism and its consequences and a relatively low value on avoiding the bleeding risk and inconvenience associated with OAC therapy.

2. In patients with rheumatic mitral valve disease and normal sinus rhythm with a left atrial diameter <5.5 cm, the guideline developers suggest clinicians not use antithrombotic therapy (Grade 2C).

Patients Undergoing Mitral Valvuloplasty

1. For patients undergoing mitral valvuloplasty, the guideline developers suggest anticoagulation with vitamin K antagonists with a target INR of 2.5 (range, 2.0 to 3.0) for 3 weeks prior to the procedure and for 4 weeks after the procedure (Grade 2C).

Mitral Valve Prolapse (MVP)

1. In people with MVP who have not experienced systemic embolism, unexplained transient ischemic attacks (TIAs), or AF, the guideline developers recommend against any antithrombotic therapy (Grade 1C).

2. In patients with MVP who have documented but unexplained TIAs, the guideline developers recommend long-term aspirin therapy, 50 to 162 mg/d (Grade 1A).
3. In patients with MVP who have documented systemic embolism or recurrent TIAs despite aspirin therapy, the guideline developers suggest long-term vitamin K antagonist therapy (target INR, 2.5; range, 2.0 to 3.0) [Grade 2C].

Mitral Annular Calcification (MAC)

1. In patients with MAC complicated by systemic embolism, not documented to be calcific embolism, the guideline developers suggest treatment with long-term OAC therapy (target INR, 2.5; INR range, 2.0 to 3.0) [Grade 2C].

Aortic Valve and Aortic Arch Disorders

1. In patients with aortic valve disease, the guideline developers suggest that clinicians not use long-term vitamin K antagonist therapy unless they have another indication for anticoagulation (Grade 2C).
2. The guideline developers suggest OAC therapy in patients with mobile aortic atheromas and aortic plaques >4 mm as measured by transesophageal echocardiography (TEE) [Grade 2C].

Prosthetic Heart Valves - Mechanical Prosthetic Heart Valves

1. For all patients with mechanical prosthetic heart valves, the guideline developers recommend vitamin K antagonists (Grade 1C+). The guideline developers suggest administration of unfractionated heparin or low molecular weight heparin (LMWH) until the INR is stable and at a therapeutic level for 2 consecutive days (Grade 2C).
2. For patients with a St. Jude Medical bileaflet valve in the aortic position, the guideline developers recommend a target INR of 2.5 (range 2.0 to 3.0) [Grade 1A].
3. For patients with tilting disk valves and bileaflet mechanical valves in the mitral position, the guideline developers recommend a target INR of 3.0 (range 2.5 to 3.5) [Grade 1C+].
4. For patients with CarboMedics bileaflet valve or Medtronic Hall tilting disk mechanical valves in the aortic position, normal left atrium size, and sinus rhythm, the guideline developers recommend a target INR of 2.5 (range 2.0 to 3.0) [Grade 1C+].
5. In patients who have mechanical valves and additional risk factors such as AF, myocardial infarction, left atrial enlargement, endocardial damage, and low ejection fraction, the guideline developers recommend a target INR of 3.0 (range 2.5 to 3.5), combined with low doses of aspirin, 75 to 100 mg/d (Grade 1C+).
6. For patients with caged ball or caged disk valves, the guideline developers suggest a target INR of 3.0 (range, 2.5 to 3.5) in combination with aspirin, 75 to 100 mg/d (Grade 2A).
7. For patients with mechanical prosthetic heart valves who suffer systemic embolism despite a therapeutic INR, the guideline developers recommend aspirin, 75 to 100 mg/d, in addition to vitamin K antagonists, and maintenance of the INR at a target of 3.0 (range 2.5 to 3.5) [Grade 1C+].

8. In patients with prosthetic heart valves in whom vitamin K antagonist must be discontinued, the guideline developers recommend LMWH (Grade 1C) or aspirin 80 to 100 mg/day (Grade 1C).

Prosthetic Heart Valves - Bioprosthetic Valves

First 3 Months after Valve Insertion

1. For patients with bioprosthetic valves in the mitral position, the guideline developers recommend vitamin K antagonists with a target INR of 2.5 (range 2.0 to 3.0) for the first 3 months after valve insertion (Grade 1C+).
2. For patients with bioprosthetic valves in the aortic position, the guideline developers suggest vitamin K antagonists with a target INR of 2.5 (range 2.0 to 3.0) for the first 3 months after valve insertion (Grade 2C) or aspirin 80 to 100 mg/day (Grade 1C).
3. In patients who have undergone valve replacement, the guideline developers suggest heparin (low molecular weight or unfractionated) until the INR is stable at therapeutic levels for 2 consecutive days (Grade 2C).
4. For patients with bioprosthetic valves who have a history of systemic embolism, the guideline developers recommend vitamin K antagonists for 3 to 12 months (Grade 1C).
5. In patients with bioprosthetic valves who have evidence of a left atrial thrombus at surgery, the guideline developers recommend vitamin K antagonists with a dose sufficient to prolong the INR to a target of 2.5 (range 2.0 to 3.0) (Grade 1C).

   Values and preferences: This recommendation places a relatively high value on preventing thromboembolic events and a relatively lower value on bleeding complications.

Long-Term Treatment

1. In patients with bioprosthetic valves who have AF, the guideline developers recommend long-term treatment with vitamin K antagonists with a target INR of 2.5 (range 2.0 to 3.0) [Grade 1C+].
2. For patients with bioprosthetic valves who are in sinus rhythm and do not have AF, the guideline developers recommend long-term therapy with aspirin, 75 to 100 mg/d (Grade 1C+).

Infective Endocarditis and Nonbacterial Thrombotic Endocarditis (NBTE)

1. In patients with a mechanical prosthetic valve and endocarditis who have no contraindications, the guideline developers suggest continuation of long-term vitamin K antagonists (Grade 2C).
2. For patients with NBTE and systemic or pulmonary emboli, the guideline developers recommend treatment with full-dose unfractionated intravenous or subcutaneous heparin (Grade 1C).
3. For patients with disseminated cancer or debilitating disease with aseptic vegetations, the guideline developers suggest administration of full-dose unfractionated heparin (Grade 2C).

Definitions

Grade of Recommendation	Clarity of Risk/Benefit	Methodological Strength of Supporting Evidence	Implications
1A	Clear	Randomized controlled trials (RCTs) without important limitations	Strong recommendation; can apply to most patients in most circumstances without reservation
1C+	Clear	No RCTs, but strong RCT results can be unequivocally extrapolated, or overwhelming evidence from observational studies	Strong recommendation; can apply to most patients in most circumstances
1B	Clear	RCTs with important limitations (inconsistent results, methodological flaws*)	Strong recommendation; likely to apply to most patients
1C	Clear	Observational studies	Intermediate-strength recommendation; may change when stronger evidence is available
2A	Unclear	RCTs without important limitations	Intermediate-strength recommendation; best action may differ depending on circumstances or patients' or societal values

Grade of Recommendation	Clarity of Risk/Benefit	Methodological Strength of Supporting Evidence	Implications
2C+	Unclear	No RCTs, but strong RCT results can be unequivocally extrapolated, or overwhelming evidence from observational studies	Weak recommendation; best action may differ depending on circumstances or patients' or societal values
2B	Unclear	RCTs with important limitations (inconsistent results, methodological flaws*)	Weak recommendation; alternative approaches likely to be better for some patients under some circumstances
2C	Unclear	Observational studies	Very weak recommendation; other alternatives may be equally reasonable

*These situations include RCTs with both lack of blinding and subjective outcomes, where the risk of bias in measurement of outcomes is high, or RCTs with large loss to follow-up.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate management of antithrombotic therapy in the various forms of valvular heart disease may reduce the risk of systemic embolism while minimizing cost and the potential for adverse events, such as bleeding.

POTENTIAL HARMS

Antithrombotic therapy, particularly with coumarin derivatives or heparin, carries a substantial risk of bleeding; this risk varies with the drug used, the intensity of the anticoagulant effect, and the clinical circumstances in individual patients.

Subgroups Most Likely to be Harmed:

Risks of anticoagulant therapy are greater in patients with endocarditis, pregnancy, and bleeding diatheses.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

Interpreting the Recommendations

- Clinicians, third-party payers, institutional review committees, or the courts should not construe these guidelines in any way as absolute dictates. In general, anything other than a Grade 1A recommendation indicates that the article authors acknowledge that other interpretations of the evidence, and other clinical policies, may be reasonable and appropriate. Even Grade 1A recommendations will not apply to all circumstances and all patients. For instance, the guideline developers have been conservative in their considerations of cost and have seldom downgraded recommendations from Grade 1 to Grade 2 on the basis of expense. As a result, in jurisdictions in which resource constraints are severe, alternative allocations may serve the health of the public far better than some of the interventions that are designated as Grade 1A. This will likely be true for all less industrialized countries and, with the increasing promotion of expensive drugs with marginal benefits, may be increasingly true for wealthier nations.
- Similarly, following Grade 1A recommendations will at times not serve the best interests of patients with atypical values or preferences or of those whose risks differ markedly from those of the usual patient. For instance, consider patients who find anticoagulant therapy extremely aversive, either because it interferes with their lifestyle (e.g., prevents participation in contact sports) or because of the need for monitoring. Clinicians may reasonably conclude that following some Grade 1A recommendations for anticoagulation therapy for either group of patients will be a mistake. The same may be true for patients with particular comorbidities (e.g., a recent gastrointestinal bleed or a balance disorder with repeated falls) or other special circumstances (e.g., very advanced age) that put them at unusual risk.
- The guideline developers trust that these observations convey their acknowledgment that no recommendations or clinical practice guidelines can take into account the often compelling and unique features of individual clinical circumstances. No clinician, and no body charged with evaluating a

clinician´s actions, should attempt to apply these recommendations in a rote or blanket fashion.

Limitations of Guideline Development Methods

The limitations of these guidelines include the possibility that some authors followed this methodology more closely than others, although the development process was centralized and supervised by the editors. Second, it is possible that the guideline developers missed relevant studies despite the comprehensive searching process. Third, the guideline developers did not centralize the methodological evaluation of all studies to facilitate uniformity in the validity assessments of the research incorporated into these guidelines. Fourth, if high-quality meta-analyses were unavailable, the guideline developers did not statistically pool primary study results using meta-analysis. Finally, sparse data on patient preferences and values, resources, and other costs represent additional limitations that are inherent to most guideline development methods.

Long-term Anticoagulant Therapy in a Patient with Valvular Heart Disease

The decision to initiate long-term anticoagulant therapy in a patient with valvular heart disease is frequently difficult because of the many variables that influence the risks of thromboembolism and of bleeding in a given individual. The patient's age, the specific valve lesion, the heart rhythm, the duration of the valve disease, a history of thromboembolism, patient attitude and lifestyle, associated diseases, and medications all must be considered. In addition to these factors, for patients who have a prosthetic heart valve, the location as well as the type of valve need to be considered. Because the state of such variables may change with time, a proper decision at one time in a patient's life may be inappropriate at another time. In some instances, the literature on a given subject is sparse or contains conflicting data that further confound the issue. Since the database for these guidelines is constantly being modified, particularly as a consequence of new randomized clinical trials (RCTs), the clinician would do well to review his or her decision at frequent intervals.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

Guideline Implementation Strategies

A full review of implementation strategies for practice guidelines is provided in the companion document titled "Antithrombotic and Antithrombolytic Therapy: From Evidence to Application." The review suggests that there are few implementation strategies that are of unequivocal, consistent benefit, and that are clearly and consistently worth resource investment. The following is a summary of the recommendations (see "Major Recommendations" for a definition of the recommendation grades).

To encourage uptake of guidelines, the guideline developers recommend that appreciable resources be devoted to distribution of educational material (Grade 2B).

They also suggest that:

- Few resources be devoted to educational meetings (Grade 2B)
- Few resources be devoted to educational outreach visits (Grade 2A)
- Appreciable resources be devoted to computer reminders (Grade 2A)
- Appreciable resources be devoted to patient-mediated interventions to encourage uptake of the guidelines (Grade 2B)
- Few resources be devoted to audit and feedback (Grade 2B)

IMPLEMENTATION TOOLS

Patient Resources
Personal Digital Assistant (PDA) Downloads
Quick Reference Guides/Physician Guides
Resources
Slide Presentation
Tool Kits

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness
Staying Healthy

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Salem DN, Stein PD, Al-Ahmad A, Bussey HI, Horstkotte D, Miller N, Pauker SG. Antithrombotic therapy in valvular heart disease--native and prosthetic: the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. Chest 2004 Sep;126(3 Suppl):457S-82S. [234 references] PubMed

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2001 Jan (revised 2004 Sep)

GUIDELINE DEVELOPER(S)

American College of Chest Physicians - Medical Specialty Society

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GUIDELINE COMMITTEE

American College of Chest Physicians Consensus Panel on Antithrombotic and Thrombolytic Therapy

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Dr. Salem has received an honorarium for speaking for Sanofi-Synthelabo-Organon.

Dr. Stein received honoraria for speaking at educational events from Aventis Pharma and Dupont Pharma. He was a consultant for Shiley several years ago.

Dr. Al-Ahmad has nothing to declare.

Dr. Bussey has received research funding from Aventis, Organon-Sanofi-Synthelabo, AstraZeneca, Bristol-Myers Squibb, Bertek Pharmaceuticals, and Novartis and has participated on advisory boards and/or research steering committees for Aventis, Organon-Sanofi-Synthelabo, and AstraZeneca. He also has received speaking honoraria from and/or served as a consultant for Aventis, AstraZeneca, Bristol-Myers Squibb, and Organon-Sanofi-Synthelabo.

Dr. Stephen Pauker has received research funding from Schering-Plough, but none related to antithrombotic therapy. Dr. Pauker is a member of the Board of Regents of the American College of Physicians.

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Salem DN, Daudelin HD, Levine HJ, Pauker SG, Eckman MH, Riff J. Antithrombotic therapy in valvular heart disease. Chest 2001 Jan;119(1 Suppl):207S-219S.

Stein PD, Alpert JS, Bussey HI, Dalen JE, Turpie AG. Antithrombotic therapy in patients with mechanical and biological prosthetic heart valves. Chest 2001 Jan;119(1 Suppl):220S-227S.

GUIDELINE AVAILABILITY

Electronic copies: Available from the Chest - The Cardiopulmonary and Critical Care Journal.

Print copies: Available from the American College of Chest Physicians, Products and Registration Division, 3300 Dundee Road, Northbrook IL 60062-2348.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- The Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. Evidence-based guidelines. Northbrook, IL: ACCP, 2004 Sep.

- Methodology for guideline development for the Seventh American College of Chest Physicians Conference on Antithrombotic and Thrombolytic Therapy. Northbrook, IL: ACCP, 2004 Sep.
- Applying the grades of recommendation for antithrombotic and thrombolytic therapy: The Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. Northbrook, IL: ACCP, 2004 Sep.
- Hemorrhagic complications of anticoagulant treatment: The Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. Northbrook, IL: ACCP, 2004 Sep.
- Antithrombotic and thrombolytic therapy: from evidence to application: The Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. Northbrook, IL: ACCP, 2004 Sep.
- Platelet-active drugs: the relationships among dose, effectiveness, and side effects: The Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. Northbrook, IL: ACCP, 2004 Sep.

Electronic copies: Available from the Chest - The Cardiopulmonary and Critical Care Journal Web site.

Print copies: Available from the American College of Chest Physicians (ACCP), Products and Registration Division, 3300 Dundee Road, Northbrook IL 60062-2348.

The following is also available:

- Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy: Evidence-based guidelines; quick reference guide. Northbrook, IL: ACCP, 2004 Sep. Personal Digital Assistant (PDA) download available at ACCP Web site.

Additional implementation tools are also available:

- Clinical resource: antithrombotic and thrombolytic therapy. Northbrook, IL. ACCP, 2004. Ordering information: Available from the ACCP Web site.

PATIENT RESOURCES

The following is available:

- A patient's guide to antithrombotic and thrombolytic therapy. In: Clinical resource: antithrombotic and thrombolytic therapy. Northbrook (IL): American College of Chest Physicians (ACCP). 2004.

Ordering information is available from the ACCP Web site.

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the

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